

(D) analyzing the interaction of all or part of each of said amino acids with all or part of the remainder of said protein backbone structure to generate a set of optimized proteins sequences.

31. (Once Amended) A method executed by a computer under the control of a program, said computer including a memory for storing said program, said method comprising the steps of:

- (A) receiving a protein backbone structure with variable residue positions;
- (B) altering at least one supersecondary structure parameter value of said protein backbone structure prior to establishing a group of potential amino acids;
- (C) classifying each variable residue position as either a core, surface or boundary residue;
- (D) establishing a group of potential amino acids for each of said variable residue positions, wherein a first group for a first variable position has a first set of at least two amino acid side chains, and wherein a second group for a second variable position has a second set of at least two different amino acid side chains, and wherein said sets are different; and
- (E) analyzing the interaction of all or part of each of said amino acids with all or part of the remainder of said protein backbone structure to generate a set of optimized protein sequences.

32. (Once Amended) A method according to claim 31 or 53 wherein said analyzing step comprises a DEE computation.

33. (Once Amended) A method according to claim 30, 31 or 53 wherein said set of optimized protein sequences comprises the globally optimal protein sequence.

34. (Once Amended) A method according to claim 32 wherein said DEE computation is selected from the group consisting of original DEE and Goldstein DEE.

35. (Once Amended) A method according to claim 30, 31 or 53 wherein said analyzing step includes the use of at least one scoring function.

36. (Once Amended) A method according to claim 35 wherein said scoring function is selected from the group consisting of a van der Waals potential scoring function, a hydrogen

bond potential scoring function, an atomic solvation scoring function, an electrostatic scoring function and a secondary structure propensity scoring function.

41. (Once Amended) A method according to claim 30, 31 or 53 further comprising experimentally testing at least one member of said set.

45. (Once Amended) A method according to claim 42 further comprising the step of: testing some or all of said protein sequences from said list to produce potential energy test results.

47. (Once Amended) A recombinant protein comprising an optimized protein sequence generated by the method of claim 30, 31 or 53.

Please add the following new claims.

53. (New) A method executed by a computer under the control of a program, said computer including a memory for storing said program, said method comprising the steps of:

- (A) receiving a protein backbone structure with variable residue positions;
- (B) altering at least one supersecondary structure parameter value of said protein backbone structure prior to establishing a group of potential amino acids;
- (C) establishing a group of potential amino acids for each of said variable residue positions, wherein a first group for a first variable position has a first set of at least two amino acid side chains, and wherein a second group for a second variable position has a second set of at least two different amino acid side chains; and
- (D) analyzing the interaction of all or part of each of said amino acids with all or part of the remainder of said protein backbone structure to generate a set of optimized protein sequences.

54. (New) A method according to claim 53 wherein said first and second sets of amino acids are different.

55. (New) A method according to claim 53 wherein said first and second sets of amino acids are the same.

56. (New) A method executed by a computer under the control of a program, said computer

including a memory for storing said program, said method comprising the steps of:

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- a) receiving a protein backbone structure with variable residue positions;
  - b) altering at least one supersecondary structure parameter value of said protein backbone structure prior to establishing a group of potential rotamer positions;
  - c) establishing a group of potential rotamers for each of said variable residue positions, wherein the group for at least one variable residue position has rotamers of at least two different amino acid side chains, and wherein at least one of said amino acid side chains is from a hydrophilic amino acid; and,
  - d) analyzing the interaction of each of said rotamers with all or part of the remainder of said protein to generate a set of optimized protein sequences, wherein said analyzing step includes the use of at least one scoring function.

57. (New) A method according to claim 56 wherein said first and second sets of rotamers are different.

58. (New) A method according to claim 56 wherein said first and second sets of rotamers are the same.

59. (New) A method according to claim 56 wherein said hydrophilic amino acid is selected from the group consisting of serine, threonine, aspartic acid, asparagine, glutamine, glutamic acid, arginine, lysine, and histidine.

60. (New) A method according to claims 53 - 59 further comprising physically generating at least one member of said set of optimized protein sequences and experimentally testing said sequence for a desired function.

#### REMARKS

Claims 30-50 and 53-60 are pending in this application. Claims 2-29, 51 and 52 have been cancelled. Claims 53 - 61 have been added. Support for the addition of the new claims may be found in original claims 30 and 31 and in the Specification at page 7, lines 4-7, 18-30, page 11, lines 9-16, at page 18, lines 11-19 and page 38, lines 13-15. No new matter has been added by the above-amendments. An Appendix of Pending Claims is attached for the Examiner's convenience.